GRIP1 gene

glutamate receptor interacting protein 1

Normal Function

The *GRIP1* gene provides instructions for making a protein that is able to attach (bind) to other proteins and is important for moving (targeting) proteins to the correct location in cells. For example, the GRIP1 protein targets two proteins called FRAS1 and FREM2 to the correct region of the cell so that they can form a group of proteins known as the FRAS/FREM complex. This complex is found in the thin, sheet-like structures (basement membranes) that separate and support the cells of many tissues. The complex is particularly important during development before birth. One of its roles is to anchor the top layer of skin by connecting the basement membrane of the top layer to the layer of skin below. The FRAS/FREM complex is also involved in the proper development of certain other organs and tissues, including the kidneys, although the mechanism is unclear.

In addition, the GRIP1 protein targets necessary proteins to the junctions (synapses) between nerve cells (neurons) in the brain where cell-to-cell communication occurs. GRIP1 may also be involved in the development of neurons.

Health Conditions Related to Genetic Changes

Fraser syndrome

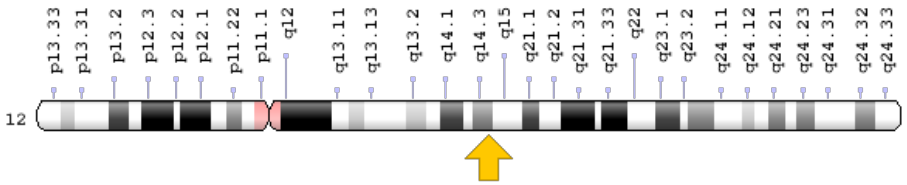
At least two *GRIP1* gene mutations have been found to cause Fraser syndrome; these mutations are involved in a small percentage of cases of this condition. Fraser syndrome affects development before birth and is characterized by eyes that are completely covered by skin (cryptophthalmos), fusion of the skin between the fingers and toes (cutaneous syndactyly), and abnormalities of the kidneys and other organs and tissues.

GRIP1 gene mutations alter the genetic blueprint that carries the instructions for making GRIP1 protein. If any GRIP1 protein is made, it is likely unable to function. Without GRIP1, FRAS1 and FREM2 do not get to the correct location to form the FRAS/FREM complex. Lack of the FRAS/FREM complex in the basement membrane of skin leads to detachment of the top layer of skin, causing blisters to form during development. These blisters likely prevent the proper formation of certain structures before birth, leading to cryptophthalmos and cutaneous syndactyly. It is unknown how lack of the FRAS/FREM complex leads to kidney abnormalities and other problems in Fraser syndrome.

Chromosomal Location

Cytogenetic Location: 12q14.3, which is the long (q) arm of chromosome 12 at position 14.3

Molecular Location: base pairs 66,347,431 to 67,069,265 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- glutamate receptor-interacting protein 1
- GRIP

Additional Information & Resources

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GRIP1%5BTIAB%5D%29+OR+%28glutamate+receptor+interacting+protein+1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- GLUTAMATE RECEPTOR-INTERACTING PROTEIN 1
  http://omim.org/entry/604597

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_GRIP1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GRIP1%5Bgene%5D
- HGNC Gene Family: PDZ domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1220

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=18708
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/23426
- UniProt
  http://www.uniprot.org/uniprot/Q9Y3R0

Sources for This Summary

- Dong H, Zhang P, Song I, Petralia RS, Liao D, Huganir RL. Characterization of the glutamate receptor-interacting proteins GRIP1 and GRIP2. J Neurosci. 1999 Aug 15;19(16):6930-41.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10436050
- OMIM: GLUTAMATE RECEPTOR-INTERACTING PROTEIN 1
  http://omim.org/entry/604597
- Heisler FF, Lee HK, Gromova KV, Pechmann Y, Schurek B, Ruschkies L, Schroeder M, Schweizer M, Kneussel M. GRIP1 interlinks N-cadherin and AMPA receptors at vesicles to promote combined cargo transport into dendrites. Proc Natl Acad Sci U S A. 2014 Apr 1;111(13):5030-5. doi: 10.1073/pnas.1304301111. Epub 2014 Mar 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24639525
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3977296/
- Schanze D, Kayserili H, Satkin BN, Altunoglu U, Zenker M. Fraser syndrome due to mutations in GRIP1--clinical phenotype in two families and expansion of the mutation spectrum. Am J Med Genet A. 2014 Mar;164A(3):837-40. doi: 10.1002/ajmg.a.36343. Epub 2013 Dec 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24357607
- Short K, Wiradjaja F, Smyth I. Let's stick together: the role of the Fras1 and Frem proteins in epidermal adhesion. IUBMB Life. 2007 Jul;59(7):427-35. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17654118
- Takamiya K, Kostourou V, Adams S, Jadeja S, Chalepakis G, Scambler PJ, Huganir RL, Adams RH. A direct functional link between the multi-PDZ domain protein GRIP1 and the Fraser syndrome protein Fras1. Nat Genet. 2004 Feb;36(2):172-7. Epub 2004 Jan 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14730302
- Vogel MJ, van Zon P, Brueton L, Gijzen M, van Tuil MC, Cox P, Schanze D, Kariminejad A, Ghaderi-Sohi S, Blair E, Zenker M, Scambler PJ, Ploos van Amstel HK, van Haelst MM. Mutations in GRIP1 cause Fraser syndrome. J Med Genet. 2012 May;49(5):303-6. doi: 10.1136/jmedgenet-2011-100590. Epub 2012 Apr 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22510445

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/GRIP1

Reviewed: June 2014
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services